



## PIK3CD gene

phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta

### Normal Function

The *PIK3CD* gene provides instructions for making the p110 delta (p110 $\delta$ ) protein, which is one piece (subunit) of an enzyme called phosphatidylinositol 3-kinase (PI3K).

The version of PI3K containing the p110 $\delta$  subunit, called PI3K-delta, is specifically found in white blood cells, including immune system cells (lymphocytes) called B cells and T cells. These cells recognize and attack foreign invaders, such as viruses and bacteria, to prevent infection.

Like other kinases, PI3K-delta adds a cluster of oxygen and phosphorus atoms (a phosphate group) to other proteins through a process called phosphorylation. PI3K-delta phosphorylates certain signaling molecules, which triggers a series of additional reactions that transmit chemical signals within cells. In lymphocytes, PI3K-delta signaling is important for many cell activities, including cell growth and division (proliferation) and maturation (differentiation). PI3K-delta helps direct B cells and T cells to differentiate into different types, each of which has a distinct function in the immune system.

### Health Conditions Related to Genetic Changes

#### activated PI3K-delta syndrome

At least four mutations in the *PIK3CD* gene have been found to cause a form of immunodeficiency called activated PI3K-delta syndrome. Immunodeficiencies are conditions in which the immune system is not able to protect the body effectively from foreign invaders such as bacteria and viruses. People with activated PI3K-delta syndrome typically have recurrent bacterial infections of the respiratory tract and chronic viral infections.

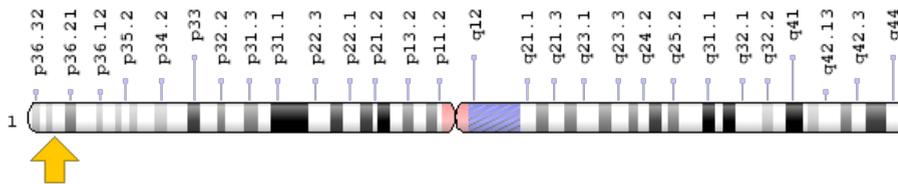
The *PIK3CD* gene mutations involved in activated PI3K-delta syndrome change single protein building blocks (amino acids) in the p110 $\delta$  protein; the most common mutation replaces the amino acid glutamic acid with the amino acid lysine at position 1021 of the protein (written as Glu1021Lys or E1021K). A PI3K-delta enzyme containing the altered p110 $\delta$  subunit is abnormally turned on (activated). Studies indicate that this overactive signaling causes T cells to mature and die too quickly. The excess signaling also blocks maturation of B cells at an early stage; the immature B cells cannot respond to foreign invaders and likely self-destruct. Lack of T cells and B cells makes it difficult for people with this disorder to fight off

bacterial and viral infections. Overactivation of PI3K-delta signaling can also stimulate abnormal proliferation of lymphocytes, and accumulation of these cells can lead to enlarged lymph nodes (lymphadenopathy). Activated PI3K-delta syndrome also increases the risk of developing a form of cancer called B-cell lymphoma.

### Chromosomal Location

Cytogenetic Location: 1p36.22, which is the short (p) arm of chromosome 1 at position 36.22

Molecular Location: base pairs 9,629,889 to 9,729,114 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### Other Names for This Gene

- APDS
- IMD14
- p110D
- P110DELTA
- phosphatidylinositol-4,5-bisphosphate 3-kinase 110 kDa catalytic subunit delta
- phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta isoform
- phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform
- phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit delta
- phosphoinositide-3-kinase C
- phosphoinositide-3-kinase, catalytic, delta polypeptide variant p37delta
- PI3-kinase p110 subunit delta
- PI3K
- PI3Kdelta
- ptdIns-3-kinase subunit p110-delta

## **Additional Information & Resources**

### Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): PI3-Kinase Produces Inositol Phospholipid Docking Sites in the Plasma Membrane  
[https://www.ncbi.nlm.nih.gov/books/NBK26822/#\\_A2861\\_](https://www.ncbi.nlm.nih.gov/books/NBK26822/#_A2861_)

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28PIK3CD%5BTIAB%5D%29+OR+%28%28P110DELTA%5BTIAB%5D%29+OR+%28PI3Kdelta%5BTIAB%5D%29+OR+%28P110D%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

### OMIM

- PHOSPHATIDYLINOSITOL 3-KINASE, CATALYTIC, DELTA  
<http://omim.org/entry/602839>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
<http://atlasgeneticsoncology.org/Genes/PIK3CDID46261ch1p36.html>
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=PIK3CD%5Bgene%5D>
- HGNC Gene Family: Phosphatidylinositol 3-kinase subunits  
<http://www.genenames.org/cgi-bin/genefamilies/set/831>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=8977](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=8977)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/5293>
- UniProt  
<http://www.uniprot.org/uniprot/O00329>

## Sources for This Summary

- Angulo I, Vadas O, Garçon F, Banham-Hall E, Plagnol V, Leahy TR, Baxendale H, Coulter T, Curtis J, Wu C, Blake-Palmer K, Perisic O, Smyth D, Maes M, Fiddler C, Juss J, Cilliers D, Markelj G, Chandra A, Farmer G, Kielkowska A, Clark J, Kracker S, Debré M, Picard C, Pellier I, Jabado N, Morris JA, Barcenas-Morales G, Fischer A, Stephens L, Hawkins P, Barrett JC, Abinun M, Clatworthy M, Durandy A, Doffinger R, Chilvers ER, Cant AJ, Kumararatne D, Okkenhaug K, Williams RL, Condliffe A, Nejentsev S. Phosphoinositide 3-kinase  $\delta$  gene mutation predisposes to respiratory infection and airway damage. *Science*. 2013 Nov 15;342(6160):866-71. doi: 10.1126/science.1243292. Epub 2013 Oct 17.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/24136356>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3930011/>
- Crank MC, Grossman JK, Moir S, Pittaluga S, Buckner CM, Kardava L, Agharahimi A, Meuwissen H, Stoddard J, Niemela J, Kuehn H, Rosenzweig SD. Mutations in PIK3CD can cause hyper IgM syndrome (HIGM) associated with increased cancer susceptibility. *J Clin Immunol*. 2014 Apr;34(3):272-6. doi: 10.1007/s10875-014-0012-9. Epub 2014 Mar 8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/24610295>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4159085/>
- Jou ST, Chien YH, Yang YH, Wang TC, Shyur SD, Chou CC, Chang ML, Lin DT, Lin KH, Chiang BL. Identification of variations in the human phosphoinositide 3-kinase p110delta gene in children with primary B-cell immunodeficiency of unknown aetiology. *Int J Immunogenet*. 2006 Oct;33(5):361-9.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16984281>
- Kracker S, Curtis J, Ibrahim MA, Sediva A, Salisbury J, Campr V, Debré M, Edgar JD, Imai K, Picard C, Casanova JL, Fischer A, Nejentsev S, Durandy A. Occurrence of B-cell lymphomas in patients with activated phosphoinositide 3-kinase  $\delta$  syndrome. *J Allergy Clin Immunol*. 2014 Jul;134(1):233-6. doi: 10.1016/j.jaci.2014.02.020. Epub 2014 Apr 1.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/24698326>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4671279/>
- Lucas CL, Kuehn HS, Zhao F, Niemela JE, Deenick EK, Palendira U, Avery DT, Moens L, Cannons JL, Biancalana M, Stoddard J, Ouyang W, Frucht DM, Rao VK, Atkinson TP, Agharahimi A, Hussey AA, Folio LR, Olivier KN, Fleisher TA, Pittaluga S, Holland SM, Cohen JI, Oliveira JB, Tangye SG, Schwartzberg PL, Lenardo MJ, Uzel G. Dominant-activating germline mutations in the gene encoding the PI(3)K catalytic subunit p110 $\delta$  result in T cell senescence and human immunodeficiency. *Nat Immunol*. 2014 Jan;15(1):88-97. doi: 10.1038/ni.2771. Epub 2013 Oct 28.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/24165795>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4209962/>
- Okkenhaug K. Signaling by the phosphoinositide 3-kinase family in immune cells. *Annu Rev Immunol*. 2013;31:675-704. doi: 10.1146/annurev-immunol-032712-095946. Epub 2013 Jan 16. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/23330955>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4516760/>
- OMIM: PHOSPHATIDYLINOSITOL 3-KINASE, CATALYTIC, DELTA  
<http://omim.org/entry/602839>

---

Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/gene/PIK3CD>

Reviewed: July 2014

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications

U.S. National Library of Medicine

National Institutes of Health

Department of Health & Human Services